

Hemispheric asymmetry and regional differences in electroencephalographic alpha activity at the wake-sleep transition

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Abstract: Electroencephalographic (EEG) alpha activity at the wake-sleep transition was studied in six right-handed adults in terms of hemispheric asymmetry and regional differences. Twelve-channel EEGs with linked mastoid references were recorded together with horizontal and vertical electro-oculograms (EOGs). Two types of alpha coefficient were obtained every 5.12 s by computing the relative proportion of right vs. left alpha band power and of anterior vs. posterior alpha band power. Four stages were scored using EEG sleep patterns (theta waves, vertex sharp waves, spindles, and K complex) and slow eye movement (SEM): stage W had neither EEG sleep patterns nor SEM; stage D1 had SEM and no EEG sleep patterns; stage D2 had theta waves or vertex sharp waves and SEM; stage S had spindles or K complex without SEM. It was found that the two types of alpha coefficient changed as a function of EEG-EOG stage and were correlated. Right-decreased and anterior-shifted alpha activities were manifest at stages D2 and S. Drowsiness was considered to be a heterogeneous state, exhibiting different spatial changes in alpha activity between stages D1 and D2.

Key words: alpha activity, hemispheric asymmetry, regional differences, drowsiness, slow eye movements.

A commonly accepted view of the electroencephalogram (EEG) at the wake-sleep transition is that alpha activity decreases, becomes intermittent and then disappears, followed by relatively low-voltage, intermixed waves and later by vertex sharp waves. In spite of the increasing interest in asymmetric alpha activity during waking, less attention has been paid to the spatial changes in alpha activity at the

wake-sleep transition. In some earlier studies, anterior-shifted alpha activity was observed with a general decrease in alpha amplitude (Gastaut & Broughton, 1965; Kojima, Shimazono, Ichise, Atsumi, Ando, & Ando, 1981; Westmoreland, 1982).

A classification system for EEG patterns in states of drowsiness offered by Santamaria and Chiappa (1987) provides a new perspective on

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alpha activity in terms of changes in spatial distribution. According to their system, the first drowsy period running between alpha patterns in wakefulness and the absence of alpha patterns is characterized by EEG transitional patterns consisting of the first recognizable alpha activity in the centrofrontal regions and the persisting alpha activity on the left temporal side. The former activity seems to be in accord with the anterior-shifted alpha activity observed in earlier studies. The latter, left-sided activity was also seen in the occipital region at the second drowsy period, with a progressive decrease in alpha amplitude. These left-sided alpha activities suggest a possible EEG asymmetry at the wake-sleep transition. Unfortunately, the system of Santamaria and Chiappa (1987) relies exclusively on visual and episodic observation and does not allow quantification of overall EEG spatial dynamics at the wake-sleep transition.

The EEG asymmetry index, calculated as ratios from the frequency content across different sites on the scalp, has been used as an objective measure of EEG spatial distribution changes during sleep. Murri and his colleagues reviewed a number of studies in which various asymmetry indexes were examined over the frontocentral regions of both hemispheres during sleep (Murri, Bonanni, Stefanini, Goldstein, Navona, & Denoth, 1992). Those studies revealed a significant reduction in the right/left ratio of total and single-frequency band power during stage 2 and periods of rapid eye movements (REM) in right-handed subjects. On the other hand, EEG spatial distribution at the wake-sleep transition has been studied in terms of regional differences rather than hemispheric asymmetry. The regional ratio, expressed as the relative proportion of anterior vs. posterior alpha band power, has been found to increase significantly as a function of EEG stage during the hypnagogic state (Tanaka, Hayashi, & Hori, 1993). A similar tendency can be seen for the alpha amplitude ratio of central vs. occipital regions when the awake EEG passed into spindle and delta patterns (Shiotsuka et al., 1991). Hemispheric asymmetry of alpha activity at the wake-sleep transition still remains to be examined.

There are a few methodological problems with the asymmetry index. First, there is no uniform formula for it. Among a number of different formulae, the ratio or coefficient for computing the relative proportion of left vs. right hemisphere EEG, $(L - R)/(L + R)$, has the most straightforward interpretation in terms of the asymmetry index and is closer to a normal distribution (Nuwer, 1988; Pivik et al., 1993). The formula was modified for computing the regional ratio of hypnagogic EEG in the work of Tanaka et al. (1993). Secondly, the asymmetry index is indicative of greater relative one-sided activation and masks the individual contributions of each hemisphere to the effect in question (Davidson, 1988). It is impossible to determine whether the ratio $(L - R)/(L + R)$ reflects increased right-hemisphere activation or decreased left-hemisphere activation or a combination of the two. Thus, additional examination of the absolute strength of EEG activity in each hemisphere is desirable.

In the present study, alpha activity at the wake-sleep transition was examined for the first time in terms of hemispheric asymmetry and regional (anterior vs. posterior) differences. For this purpose, two types of alpha coefficients were computed as the relative proportion of alpha band power.

The wake-sleep transition (so-called "drowsiness") is situated around the center of a continuum of arousal level. The EEG-based criterion defines stage 1, or drowsiness, as a decrease in the amount of alpha activity in a given epoch (Rechtschaffen & Kales, 1968). The application of this criterion, however, is limited to those subjects who produce abundant alpha activity. If applied to the alpha-poor subjects, this criterion would result in a misleading assessment of drowsiness. There is increasing agreement that slow eye movement (SEM) serves as a reliable alternative for assessing drowsiness (Hori, 1982; Kojima et al., 1981; Ogilvie & Wilkinson, 1984; Ogilvie, McDonagh, & Stone, 1988; Santamaria & Chiappa, 1987). One of the present authors has found a significant linkage of SEM with lower levels of arousal, such as sleepiness, with the transitional period of sleep stage, and with difficulty in falling asleep

(Hiroshige, 1987, 1992; Hiroshige & Miyata, 1990). Moreover, the stage defined by the EEG and electro-oculogram (EOG) (EEG-EOG stage) is helpful for the recognition of a drowsy state even in EEG-defined wakefulness. For instance, stage alpha-SEM (alpha accompanied by SEMs) was distinguished from stage alpha-REM (alpha accompanied by REM) in the incidence of hallucinatory reports (Foulkes & Vogel, 1965). In the present study, four categories of EEG-EOG stage were employed to describe the wake-sleep transition. Hemispheric asymmetry and regional differences in alpha activity were analyzed with respect to EEG-EOG stage.

Method

Subjects

Six right-handed volunteers (five female and one male), ranging in age from 19 to 35 years, participated in this study. They were free from any signs of serious psychological disturbance and difficulty in sleep. Data on three additional subjects were excluded from analysis because of apparatus failure and recordings contaminated by electromyographic activity.

Procedures for recording

Twelve EEG active scalp electrodes were applied on sites F₃, F₄, C₃, C₄, P₃, P₄, O₁, O₂, T₃, T₄, T₅, T₆ with linked mastoid references according to the 10–20 International System. The midline sites were not included because one of the primary goals was to study hemispheric asymmetry. Neither Fp₁ nor Fp₂ were used because EEG records on frontal poles were apt to be contaminated by blinks and eye movements. Horizontal EOGs were monopolarly recorded from both outer canthi of the eyes with ipsilateral mastoid references. Vertical EOG was bipolarly recorded from above and below the orbit of the right eye. The EEG and vertical EOG signals were amplified with the upper frequency limit set at 30 Hz and the time constant at .3 s. Horizontal EOG signals were amplified with the upper frequency limit set at 15 Hz and the time constant at 3.0 s.

The experiments were undertaken between 15:00 and 17:00 with a recording duration of about 40 min. An IBM PC-compatible CARTOGRAPH MOZGA system, developed by the Scientific Medical Center of Moscow, "GEYA," was used to collect, store, analyze and display EEG and EOG data. The system was secured while each subject sat in a reclining chair, with electrodes attached, in a reasonably sound-proof and electrically shielded room. Each subject was instructed to recline, relaxed, with eyes closed. They were each informed that, should they fall asleep, they would be awakened by an experimenter entering the room to ask them to assess their sleepiness. The light was turned off and recording was begun. The subjects were awakened once and asked to assess their sleepiness (Hoddes, Zarcone, Smythe, Phillips, & Dement, 1973) after their EEG records revealed spindles or K complex patterns. Following the completion of an assessment of sleepiness, the subjects were allowed to doze off once more and the recording was begun again.

Data sampling and processing

All amplified signals were digitized with a 12-bit analogue-digital converter every successive 5.12-s epoch at a sampling rate of 100 Hz. Then EEG power spectra with a resolution of .195 Hz were computed using FFT procedures for all of the 2,411 epochs that were artifact free, and alpha band power (7.42–11.91 Hz) was analyzed. In order to evaluate hemispheric asymmetry and regional differences, two types of alpha coefficient were computed every 5.12 s as the relative proportion of right-hemisphere vs. left-hemisphere alpha band power and of anterior vs. posterior alpha band power, using the formulae $(R - L)/(R + L)$ and $(A - P)/(A + P)$. R was an averaged power summed over the right sites F₄, C₄, P₄, T₄, T₆ and O₂; L was calculated from the left sites F₃, C₃, P₃, T₃, T₅ and O₁; A from the anterior sites F₃, F₄, C₃, C₄, T₃ and T₄; and P from the posterior sites P₃, P₄, T₅, T₆, O₁ and O₂.

Four EEG-EOG stages were scored every 5.12-s epoch using a combination of EEG sleep patterns and SEM. The EEG sleep patterns comprised the four waves designated in the

standard criteria (Rechtschaffen & Kales, 1968): low-voltage 2–7 Hz theta waves; vertex sharp waves with an amplitude of 50 μ V or greater; 12–14 Hz spindles with a duration of more than 500 ms; and K complex. Alpha waves were excluded since they were a dependent variable in the present study. The SEMs were identified as out-phase deflections of two horizontal EOGs with an excursion lasting no less than 500 ms and with an amplitude of 50 μ V or greater (Hiroshige, 1987). The criteria for scoring EEG-EOG stages were as follows: stage W was defined as the lack of both EEG asleep patterns and SEM; stage D1 was defined as the presence of SEM without EEG asleep patterns (this stage was a mixture of stage wake and the earlier phase of stage 1, according to the standard criteria, for some epochs showed the alpha wave train and others the alpha wave intermittently); stage D2 was distinguished from stage D1 by the presence of theta waves or vertex sharp waves, roughly corresponding to the later phase of standard stage 1; and stage S was defined as the presence of spindles or K complexes without SEM, nearly identical to standard stage 2.

Statistical analysis

One-way repeated-measures analyses of variance (ANOVAs) were performed separately on the alpha coefficients to test the effect of EEG-EOG stage. Two-way repeated-measures ANOVAs were also performed on alpha band power to test the effects of location (right vs. left and anterior vs. posterior), of stage and of location \times stage interaction. For all ANOVAs, Greenhouse-Geisser corrections were used to adjust the degrees of freedom when appropriate to counteract the heterogeneity of the variance-covariance matrix associated with repeated measures (Jennings & Wood, 1976). In reporting the results, only findings that reached a .05 significance level were considered. The Greenhouse-Geisser epsilon value (ϵ) and the appropriately adjusted degrees of freedom have also been provided. To test specific effects of stage and location, post-hoc comparisons using the Tukey test were made.

Results

Examples of changes in alpha band power and alpha coefficients at the wake-sleep transition

Figures 1 and 2 illustrate the time course of alpha band power and EEG coefficients with EEG-EOG stages for the hemispheres (a), and the anteroposterior regions (b), respectively, obtained from two different subjects with alpha activities asymmetric (Figure 1a) and less asymmetric (Figure 2a) during waking. Averaged powers from each hemisphere and region (top) drastically decreased during the period of frequent stages D2 and S, with occasional increases on a contingent recovery of stages W or D1. Meanwhile, power differences (second from top) approached the value of zero, indicating the loss of alpha predominance, which was situated basically in the right hemisphere and the posterior region during waking. Alpha coefficients (third) made the small amounts of power difference visible as a long-term change superimposed by a short-term fluctuation. Averaged alpha coefficients (fourth) manifested the long-term changes as a reduction in right-predominant alpha with the occasional (Figure 1a) and continuous (Figure 2a) left-sided alpha and as a shift of alpha predominance to the anterior region (Figures 1b and 2b).

Hemispheric asymmetry and regional differences at EEG-EOG stages

Table 1 summarizes the averaged alpha coefficients of hemispheric asymmetry and regional differences at the four EEG-EOG stages in terms of magnitude and incidence. The magnitude was given by the score of the alpha coefficient averaged for each stage for each subject. The incidence indicated the percentage of epochs with a positive alpha coefficient, for right and anterior predominance, obtained for each stage for each subject. The magnitude of alpha coefficients changed significantly as a function of EEG-EOG stage for hemispheric asymmetry, $F(2, 9) = 4.38, p < .05, \epsilon = .605$, and for regional difference, $F(1, 7) = 10.17, p < .02, \epsilon = .433$. Post-hoc comparisons indicated that hemispheric asymmetry declined in right

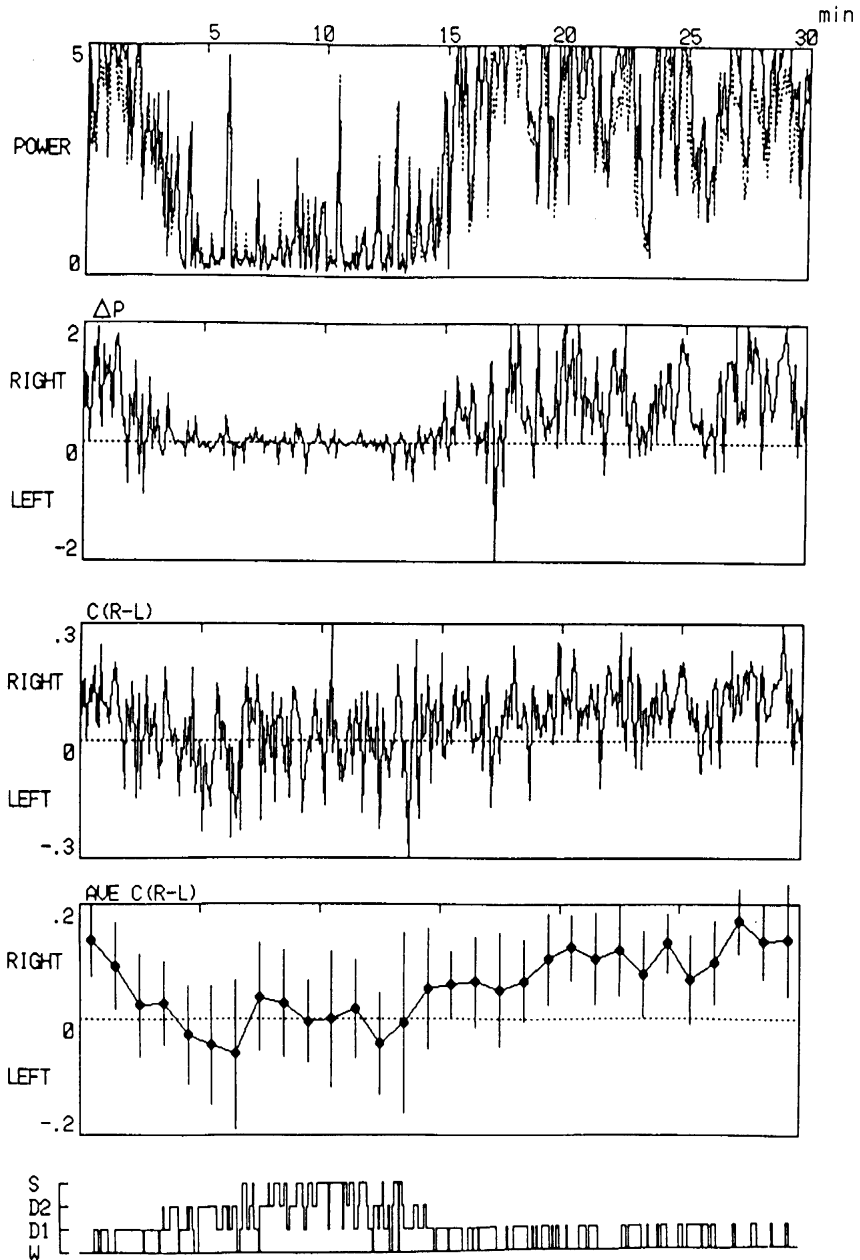


Figure 1a. Hemispheric asymmetry of EEG alpha activity at the wake-sleep transition. Power (top): averaged alpha band power from the right (solid line) and the left (dotted line) hemispheres. ΔP (second): power difference between the two hemispheres. $C(R-L)$ (third): alpha coefficient $(R-L)/(R+L)$. $AVE C(R-L)$ (fourth): 1-min averaged alpha coefficient. EEG-EOG stages at the bottom. Alpha activity during waking is asymmetric, with the right side predominant.

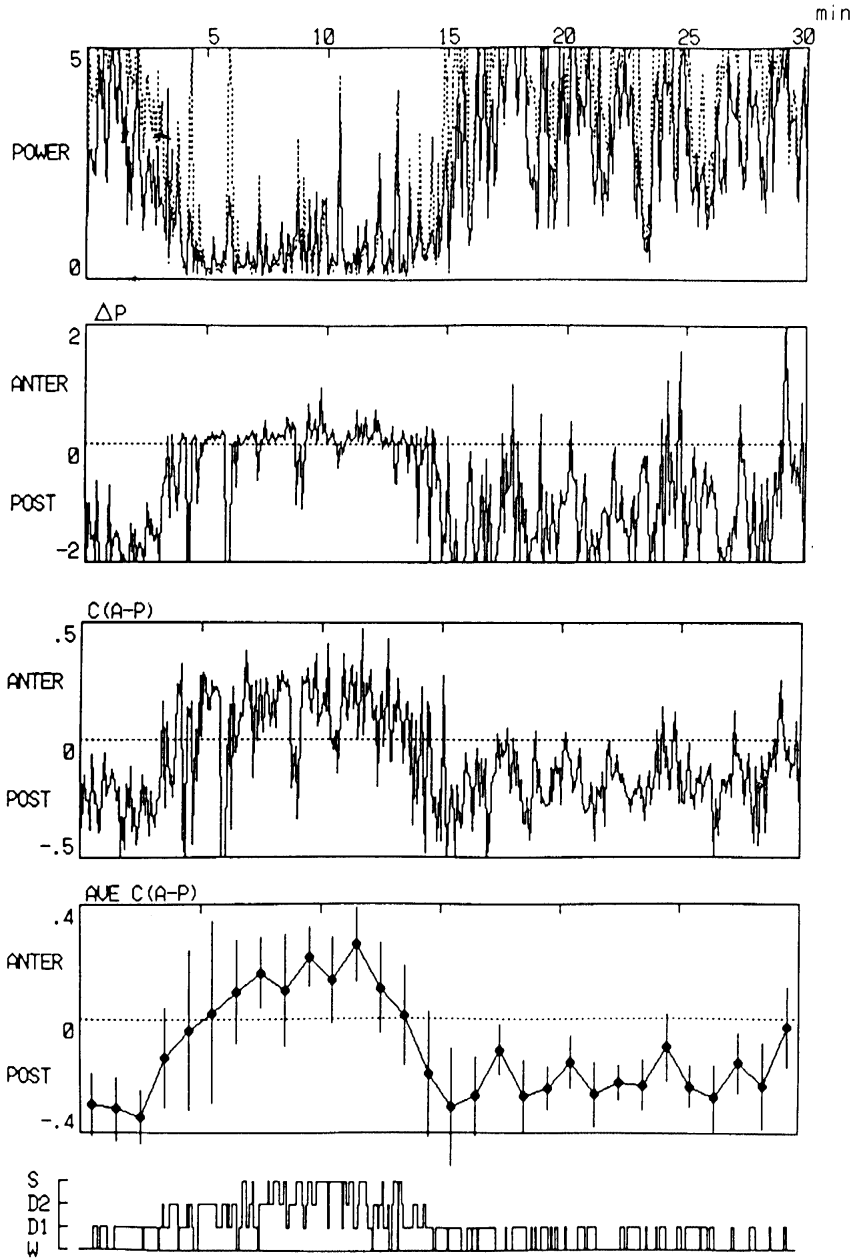


Figure 1b. Regional difference in EEG alpha activity at the wake-sleep transition, obtained from the same subject as reported in Figure 1a. Power (top): averaged alpha band power of the anterior (solid line) and the posterior (dotted line) regions. ΔP (second): power difference between the two regions. $C(A-P)$ (third): alpha coefficient $(A - P)/(A + P)$. Ave $C(A - P)$ (fourth): 1-min averaged alpha coefficient.

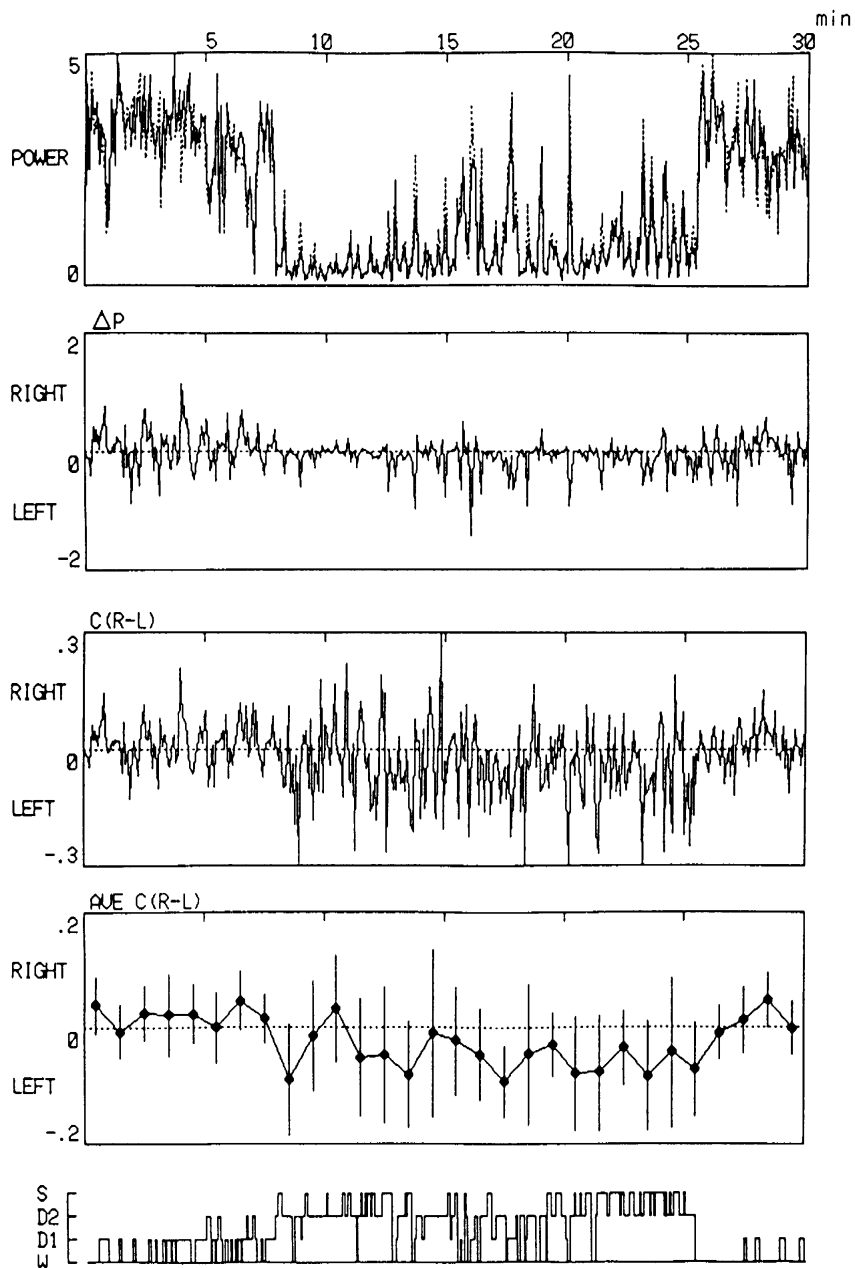


Figure 2a. Hemispheric asymmetry of EEG alpha activity at the wake-sleep transition. Note that this subject shows less asymmetric alpha activity during waking. All abbreviations are the same as in Figure 1a.

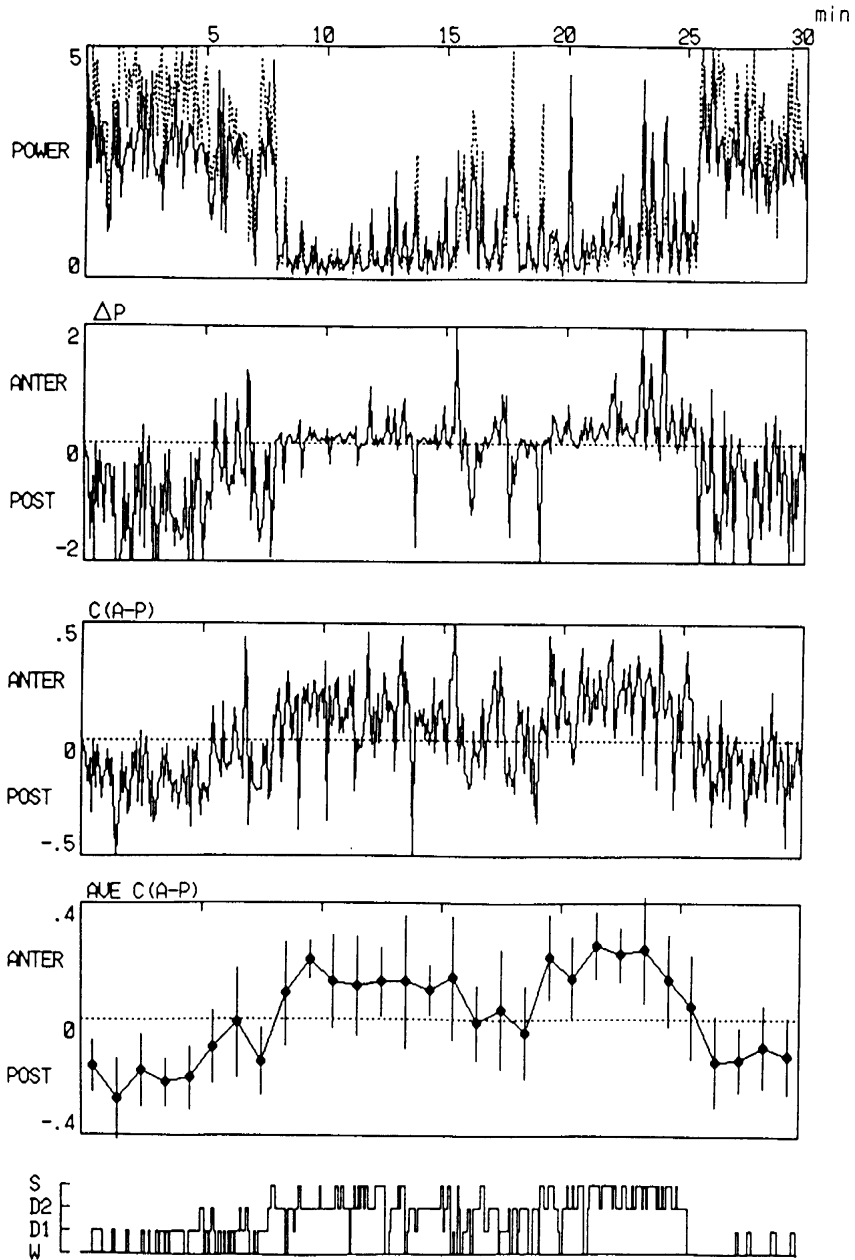


Figure 2b. Regional difference of EEG alpha activity at the wake-sleep transition, obtained from the same subject as reported in Figure 2a. All abbreviations are the same as in Figure 1b.

Table 1. Alpha coefficients of alpha band power for hemisphere asymmetry and regional differences at four EEG-EOG stages

	EEG-EOG stages			
	W	D1	D2	S
Magnitude				
(R - L)/(R + L)	.078 (.021)	.055 (.013)	.032 (.025)	.032 (.018)
(A - P)/(A + P)	-.058 (.042)	-.053 (.066)	.108 (.045)	.124 (.044)
Incidence (%)				
Right predominance	75.1 (6.4)	70.6 (4.5)	57.7 (8.2)	56.8 (7.9)
Anterior predominance	36.0 (8.9)	33.8 (11.8)	71.8 (9.0)	75.9 (8.0)

Values in parentheses indicate standard errors.

Table 2. Pearson's product-moment correlation coefficients (r) between hemispheric asymmetry and regional differences in alpha activity at the wake-sleep transition

Subject	r	t	n^1
A	-.697	5.832**	38
B	-.627	4.334**	31
C	-.680	5.246**	34
D	-.644	4.980**	37
E	-.632	4.613**	34
F	-.146	0.738	27

¹ The number of data pooled every 1 min.

** $p < .01$.

predominance at stages D2 and S, and that posterior predominance at stages W and D1 shifted to anterior predominance at stages D2 and S. The percentage incidence of anterior predominance was twice as high at stages D2 and S than at stages W and D1, $F(1, 6) = 11.28$, $p < .02$, $\epsilon = .374$. The percentage incidence of right predominance showed a tendency to be lower at stages D2 and S, $F(2, 10) = 3.90$, $p < .053$, $\epsilon = .683$.

As shown in Figures 1 and 2, the long-term changes in hemispheric asymmetry and regional differences seem to covary. To examine the degree of their correlation, Pearson's product-moment correlation coefficient was computed

for each subject using 1-min averaged values of alpha coefficients. The results are summarized in Table 2. Significant, and fairly strong, negative correlations were obtained for five of the six subjects, indicating that alpha activity at the wake-sleep transition tended to shift towards the anterior region as right predominance grew weaker.

Locations contributing to hemispheric asymmetry and regional differences in alpha activity

To examine the individual contributions of each hemisphere and region to the effects obtained in Table 1, the alpha band power was analyzed separately for each hemisphere and region. The power decreased linearly as a function of stage for hemisphere, $F(1, 6) = 12.79$, $p < .02$, $\epsilon = .407$, and for region, $F(1, 6) = 12.71$, $p < .02$, $\epsilon = .409$. No other effects were significant. Large individual differences reduced the effect of location, and further analyses were performed to normalize the alpha band power for each hemisphere and region. Normalized power was expressed as a percentage of the mean power at stage W, and was obtained for each epoch for each subject. The mean normalized powers comparing the hemispheres and the regions for different EEG-EOG stages are given in Figure 3. The effects of location

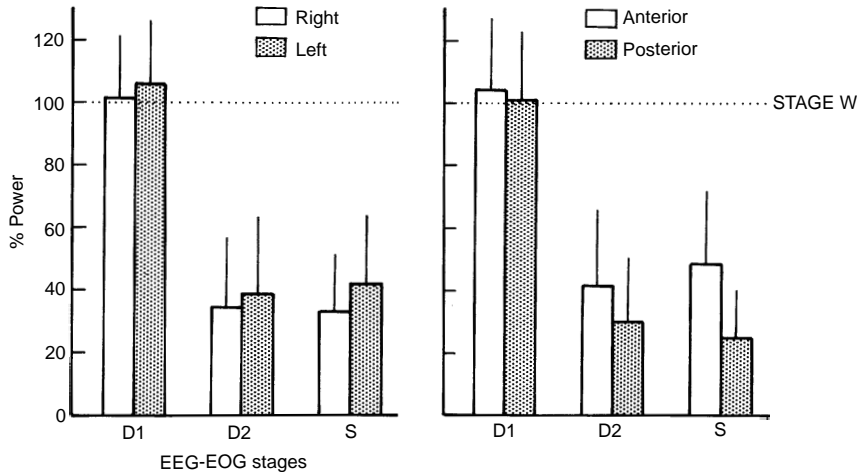


Figure 3. Comparison of normalized alpha band power between the hemispheres and between the regions at different EEG-EOG stages. Normalization of alpha band power, relative to mean power (100%) at stage W, was performed on each of the hemispheres and regions.

($F(1, 5) = 12.79, p < .02$; $F(1, 5) = 11.64, p < .02$) and stage ($F(1, 6) = 26.31, p < .01, \epsilon = .596$; $F(1, 6) = 27.10, p < .01, \epsilon = .624$) were significant for hemisphere and for region, respectively. No interactions were significant. Post-hoc comparisons indicated that a larger decrease was found in the normalized power of the right hemisphere and the posterior region, and that stage D1 was distinguished by an increased power, exceeding the reference level.

Discussion

The present study investigated the spatial distribution changes in alpha activity at the wake-sleep transition. The main finding was that hemispheric asymmetry and regional differences in alpha activity changed significantly as a function of EEG-EOG stages while the alpha band power decreased linearly.

The reduction in right-hemisphere predominance was basically characteristic of the hemispheric asymmetry of alpha activity at the wake-sleep transition. This was evidenced by the fact that the alpha coefficient $(R - L)/(R + L)$ decreased in magnitude as a function of EEG-EOG stage and that the normalized power in

the right hemisphere showed a larger decrease. Although there have been no reports that can be directly compared with the present results, hemodynamic evidence from the work of Sakai and his colleagues supports right-left asymmetry during earlier periods of sleep (Sakai, Meyer, Karacan, Derman, & Yamamoto, 1980). These authors found that the regional cerebral blood flow of human subjects decreased more in the right hemisphere than in the left at sleep stages I and II (Williams, Karacan, & Hirsch, 1974). Alpha asymmetry with the left hemisphere predominant differed among the subjects as well as within each subject (Figures 1 and 2). Such individual differences made ambiguous the effect of EEG-EOG stage on the incidence of left-side predominance, suggesting only an increasing tendency at stages D2 and S (Table 1). Similarly, our visual inspection of EEG records in the work of Santamaria and Chiappa (1987) indicated that in 57 EEG records of drowsiness, left-sided alpha activity was found in nearly as many cases as right-sided and symmetric alpha activities. This was not the case, however, with EEG records of wakefulness. Taken together, it seems reasonable to postulate that alpha activity in the right

hemisphere is sensitive to the change in arousal level. The question as to whether or not the left-predominant alpha activity at the wake-sleep transition may reflect mental processes, such as hallucination and dreaming (Foulkes & Vogel, 1965), will be examined in future studies.

Regional differences in alpha activity at the wake-sleep transition were state dependent. Alpha predominance was situated in the posterior region at stages W and D1 and in the anterior region at stages D2 and S. The latter anterior-shifted alpha activity was evidenced by the increased magnitude and incidence of the alpha coefficient $(A - P)/(A + P)$ and by the smaller decrease in normalized power in the anterior region. These results extend the previous findings arrived at by alpha index computation (Tanaka et al., 1993), visual inspection (Santamaria & Chiappa, 1987) and EEG topographic mapping (Buschsbaum et al., Hiroshige, Dorokhov, & Gaidarenko, 1991; Hori, Hayashi, & Morikawa, 1990; Tada & Katayama, 1989). Santamaria and Chiappa (1987) found large individual differences in anterior-shifted alpha activity. Such activity was the more common in 22% of their 55 subjects, was seen at least once in 75%, but was uncommon in the rest. Their observations were based on visual analysis of multichannel EEG records, which is apt to miss the small but important differences in alpha amplitude between the electrode sites. The findings of the present study are different. Four out of our six subjects exhibited clear state-dependent changes in incidence of anterior-shifted alpha activity (21–86%), while another showed low incidence (16–39%) and the last showed high incidence (68–88%) throughout the stages. Nevertheless, the alpha coefficient $(A - P)/(A + P)$ powerfully detected the anterior-shifted alpha activity in all subjects, with higher incidence at stages D2 and S (32–90%) than at stages W and D1 (16–73%), independently of the total amount of alpha band power. Further investigations with a larger sample or with repeated observations on the same subject will be necessary for a general confirmation of the results obtained using this alpha coefficient.

Another interesting finding in the present study is the significant correlation between the two types of alpha coefficient, $(R - L)/(R + L)$ and $(A - P)/(A + P)$, which was fairly strong for almost all subjects. This indicates that alpha activity at the wake-sleep transition can be expressed as a coupling of hemispheric asymmetry and regional differences, yielding a scatterplot of paired alpha coefficients against the right vs. left axis and the anterior vs. posterior axis. In our preliminary study, in which such a scatterplot was examined (Hiroshige et al., 1991), the alpha predominance was illustrated as a cluster of the paired alpha coefficients that varied from stage to stage.

The results of this study indicated drowsiness as a heterogeneous state exhibiting different spatial variations of alpha activity between stages D1 and D2. This seems to justify the division of these stages, which were manually scored depending on EEG sleep patterns, although SEM was commonly observed. In addition, Table 1 and Figure 3 suggest that stages D2 and S can be combined, and then drowsiness may be prolonged to stage S (stage 2, according to the standard criteria). A similar view was put forward by Hori (1985), who, in a study of EEG heterogeneous structures in the hypnagogic state, postulated that the hypnagogic state probably started before the onset of stage 1 and continued for several minutes after the onset of stage 2.

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